

What is claimed is:

1. A method for producing a substantially tetramer free hemoglobin solution comprising:
  - a) polymerizing hemoglobin in solution;
  - b) heat treating the polymerized hemoglobin in solution;
  - 5 c) removing tetramer from the polymerized hemoglobin in solution.
2. The method of claim 1 wherein the hemoglobin is derived from mammalian blood.
3. The method of claim 2 wherein the mammalian blood is human blood and the hemoglobin is pyridoxylated.
4. The method of claim 1 wherein the hemoglobin is derived from bovine blood.
- 10 5. The method of claim 1 wherein the hemoglobin is polymerized with glutaraldehyde.
6. The method of claim 1 wherein the tetramer is removed by filtration.
7. The method of claim 1 wherein the heat treatment comprises heating the solution above about 45° C for at least about 24 hours.
8. The method of claim 1 wherein the tetramer concentration at the completion of step (c) is  
15 less than about 1.0% of total hemoglobin in the solution.

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9. The method of claim 1 wherein the tetramer concentration at the completion of step (c) is less than about 0.3% of total hemoglobin in the solution.
  10. The method of claim 1 further comprising, in addition to step (c), removing tetramer from the solution prior to the heat treating.
  - 5 11. The method of claim 10 wherein tetramer is removed from the solution prior to the heat treating until the solution is essentially tetramer free.
  12. The method of claim 11 wherein the tetramer concentration prior to the heat treating is less than about 1.0% of total hemoglobin in the solution.
  13. The method of claim 12 wherein the tetramer concentration prior to the heat treating is less  
10 than about 0.3% of total hemoglobin in the solution.
  14. A hemoglobin solution produced by the method of claim 1.
  15. A method for stabilizing an essentially tetramer free polymerized hemoglobin solution comprising treating the polymerized hemoglobin solution to partially degrade the polymerized hemoglobin to tetramer and removing the tetramer from the solution.
  - 15 16. The method of claim 15 wherein the treating comprises aging the solution.

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17. The method of claim 15 wherein the treating comprises aging the solution until the tetramer concentration is above about 1.0 % of the total hemoglobin in solution.
18. The method of claim 15 wherein the treating comprises heating the solution.
19. The method of claim 15 wherein the treating comprises heating the solution until the  
5 tetramer concentration is above about 1.0 % of the total hemoglobin in solution.
20. The method of claim 15 wherein the hemoglobin is derived from mammalian blood.
21. The method of claim 15 wherein the mammalian blood is human blood and the hemoglobin is pyridoxylated.
22. The method of claim 15 wherein the hemoglobin is derived from bovine blood.
- 10 23. The method of claim 15 wherein the hemoglobin is polymerized with glutaraldehyde.
24. The method of claim 15 wherein the tetramer is removed by filtration.
25. The method of claim 18 wherein the heating comprises heating the solution above about 45° C for at least about 24 hours.
26. A method for producing a stabilized, polymerized hemoglobin solution comprising:

- a) producing a polymerized hemoglobin solution;
- b) removing tetramer from the polymerized hemoglobin solution to produce a substantially tetramer free polymerized hemoglobin solution;
- c) aging the polymerized hemoglobin solution; and
- 5 d) removing the elaborated tetramer.
27. The method of claim 26 wherein the aging comprises storing the hemoglobin solution until the tetramer concentration is greater than about 1.0% of total hemoglobin.
28. The method of claim 26 wherein the aging comprises storing the hemoglobin solution until the tetramer concentration is greater than about 3.0% of total hemoglobin.
- 10 29. The method of claim 26 wherein the aging comprises storing the hemoglobin solution for longer than one year.
30. A method for producing a substantially tetramer free hemoglobin solution comprising:
- e) subjecting hemoglobin in solution to a polymerization reaction comprising a polymerizing agent;
- 15 f) quenching the polymerization reaction with a quenching agent;
- g) heating the solution during the quenching;

h) removing tetramer from the polymerized hemoglobin in solution.

31. The method of claim 30 wherein the solution is heated to at least about 40° C during the quenching for at least three hours.

32. The method of claim 31 wherein the solution is heat to about 40 – 50 ° C.